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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,558	09/02/2005	Jorg Hacker	H&U122	9541

7590 09/01/2009

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EXAMINER	
JOIKE, MICHELE K	

ART UNIT	PAPER NUMBER
1636	

MAIL DATE	DELIVERY MODE
09/01/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/525,558	HACKER ET AL.	
	Examiner	Art Unit	
	MICHELE K. JOIKE	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 June 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 24, 2009 has been entered.

Claims 1-6 are pending and examined. Any rejection of record in the previous Office Action, mailed December 23, 2008 that is not addressed in this action has been withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-6 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. There is no support in the specification for substantially simultaneously introducing the altered pMut1 and pMut2 plasmids. The

specification is silent on the timing of introducing these plasmids. This is a new matter rejection.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, the plasmid-free clone of Escherichia coli strain DSM 6601 is identical to Escherichia coli strain DSM 6601. Strains contain natural variations, so it is unclear how the strains can be identical. If applicants intend for the plasmid-free clone of Escherichia coli strain DSM 6601 to be identical to a deposited Escherichia coli strain DSM 6601 that should be indicated in the claim.

Response to Arguments Concerning Claim Rejections – 35 USC § 103 (a)

Applicant's arguments filed June 24, 2009 have been fully considered and have been found persuasive for the rejection of claim 1.

The following grounds of traversal are presented:

Trevors et al cannot be cited to teach the claimed E. coli strain because the genome is identical to wild-type DSM 6601. Furthermore, they teach several methods for curing bacteria, but none of the methods equates to the method taught by the applicants. Plasmid-free clones of DSM 6601 cannot be prepared at all with normal

genetic engineering methods or can be prepared only with great difficulty. It took more than routine procedures to create plasmid-free clones of DSM 6601. Lastly a major advantage of the claimed strain is that it can readily be used as a cloning vehicle, and can be used for the treatment of disturbances of the gastrointestinal tract.

Applicant's arguments have been found persuasive for the following reasons.

Any plasmid-free clone of DSM 6601 would inherently have the same properties as the claimed strain, and Blum-Oehler teaches that DSM 6601 is useful as a probiotic drug against intestinal disorders and diseases. As discussed above, strains contain natural variations, so it is unclear how the strains can be identical, so that limitation is not being given any patentable weight. However, the argument that plasmid-free clones of DSM 6601 cannot be prepared at all with normal genetic engineering methods or can be prepared only with great difficulty is persuasive, however, a new 35 USC 103(a) rejection is made below, citing a reference teaching the method applicants used to make their plasmid-free DSM 6601 clone.

Applicant's arguments filed June 24, 2009 have been fully considered but they are not persuasive for the rejection of claims 2-6.

Applicants argue that pMut1 and pMut2 are simultaneously introduced into E. coli, which is a limitation not taught by the references. This approach allowed for the elimination of both of the cryptic plasmids in one step. This is in contrast to the transfer of plasmids by conjugation to be cured as taught by Uraji et al.

Applicant's arguments have not been found persuasive for the following reasons.

Applicants claim the substantially simultaneous introduction of the plasmids. This is not the same as simultaneous. Since there is no definition of substantially simultaneous in the specification, the Examiner is interpreting it broadly to include the introduction of plasmids as taught by the references. The plasmids do not have to be introduced at the same time, and absent evidence to the contrary, the plasmids were introduced substantially simultaneously, as there was no indication in the references of a delay for the introduction of the plasmids.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Uraji et al, in view of Blum-Oehler et al and in further view of Trevors et al.

Uraji et al (Genes Genet. Syst. 77: 1-9, 2002, specifically p. 3, including figure 1 and p. 7) teaches a curing method wherein bacteria are transformed with a plasmid containing an introduced sacB gene and an introduced kanamycin resistance cassette. The bacterium already contains a second plasmid (without the sacB gene). The bacteria is then cured of both plasmids by culturing the cells overnight in LB supplemented with sucrose (also called saccharose), and then were grown on media

supplemented with kanamycin. Uraji et al do not teach the sacB gene on the second plasmid, because the plasmid is already present in the cell. However, they do teach that sacB should be in a plasmid being introduced into the cell that is being cured. Therefore, if two plasmids are being introduced into the cell, it would follow that both plasmids would contain the sacB gene in order to cure the cell. In claim 6, the steps are the reverse of the method steps taught by Uraji et al. First, the transformed bacteria are cultivated on plates containing the antibiotic, and then subsequently on plates containing saccharose. As stated in MPEP 2144.04 (IV)(C), selection of any order of performing process steps is prima facie obvious in the absence of new or unexpected results.

> C. Changes in Sequence of Adding Ingredients
>
> *Ex parte Rubin* , 128 USPQ 440 (Bd. App. 1959) (Prior art reference disclosing a process of making a laminated sheet wherein a base sheet is first coated with a metallic film and thereafter impregnated with a thermosetting material was held to render *prima facie* obvious claims directed to a process of making a laminated sheet by reversing the order of the prior art process steps.). See also *In re Burhans*, 154 F.2d 690, 69 USPQ 330 (CCPA 1946) (selection of any order of performing process steps is *prima facie* obvious in the absence of new or unexpected results); *In re Gibson*, 39 F.2d 975, 5 USPQ 230 (CCPA 1930) (Selection of any order of mixing ingredients is *prima facie* obvious.).

However, Uraji et al do not teach the DSM 6601 strain, or the pMut plasmids, or use of a tetracylcine cassette in one of the plasmids.

Blum-Oehler et al (IDS ref., specifically pp. 59) teaches the E. coli strain, DSM 6601, which is also called Nissle 1917, which contain the pMut1 and pMut2 plasmids. However, they do not teach curing plasmids.

Trevors et al (FEMS Microbiol. Reviews 32: 149-157, 1986, specifically p. 149) teaches curing bacteria of plasmids.

The ordinary skilled artisan, desiring to have a plasmid-free clone of DSM 6601, would have been motivated to combine the teachings of Uraji et al teaching how to cure bacteria of plasmids using the sacB gene with the teachings of Blum-Oehler et al teaching the DSM 6601 strain because Trevors et al teach that it is desirable to cure bacteria of plasmids because it allows for a direct comparison of cells with and without plasmids, and one would be motivated to cure DSM 6601 because Blum-Oehler et al teach that DSM 6601 is useful as a probiotic drug against intestinal disorders and diseases, and, as taught by Blum-Oehler et al, their method is a much safer way of curing as it essentially has no effect on the host chromosome. It would have been obvious to one of ordinary skill in the art because Blum-Oehler et al teach that the plasmids (pMut1 and pMut2) are cryptic plasmids and have no apparent benefit to their host. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 2-6 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Uraji et al in view of Blum-Oehler et al, in view of Trevors et al, and in further view of Alexeyev et al. This rejection is maintained for reasons of record.

Allowable Subject Matter

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHELE K. JOIKE whose telephone number is (571)272-5915. The examiner can normally be reached on M-F, 10:00-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571)272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michele K. Joike/
Examiner, Art Unit 1636

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Examiner
Art Unit 1636